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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/671,106 | 09/25/2003 | Michael E. O'Donnell | 22221/1150 (RU-339) | 7285 |
| 7590 Nixon Peabody LLP Clinton Square P.O. Box 31051 Rochester, NY 14603-1051 | | | | |
| EXAMINER | | | | |
| HUTSON, RICHARD G | | | | |
| ART UNIT | | PAPER NUMBER | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/671,106

Applicant(s)

O'DONNELL ET AL.

Examiner

Richard G. Hutson

Art Unit

1652

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 January 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,6-9 and 12-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 17-21 is/are allowed.
- 6) ☒ Claim(s) 1,2,6-9 and 12-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/S508)
- Paper No(s)/Mail Date 1/2/2008.
- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application.
- 6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/2/2008 has been entered.

Applicant's amendment of claims 1, and the cancellation of claims 10-11, in the paper of 1/2/2008, is acknowledged. Claims 1, 2, 6-9, 12-21 are at issue and are present for examination. Applicants' arguments filed on 1/2/2008, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 6-8, 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 6-8, 12-16 are indefinite in that the reference in claim 1 to "5X sodium citrate buffer" is unclear because it is not known what exactly "5X sodium citrate buffer" is. While the use of various sodium citrate buffers in hybridization methodologies is common place in this art, it remains unclear as to what applicants recited "5X sodium citrate buffer" is and thus the breadth of the claim is unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 6-9 and 12-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous claims 1, 2, 6-16 and 20. In response to this rejection, applicants have amended claims 1, canceled claims 10-11 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse the rejection on the basis that Claim 1 presently recites that "the encoded delta prime subunit can cooperate with delta and tau/gamma subunits to form a clamp loader complex" and persons of skill in the art would appreciate that this is precisely the function attributed to delta prime subunits of polymerase III enzyme complexes (and, thus, the DNA encoding these subunits).

Applicants further submit that the encoded delta prime subunit is structurally related to other delta prime subunits as evidenced by the comparison of the *Bacillus stearothermophilus* delta prime subunit relative to other previously known delta prime subunits from *Geobacillus kaustophilus*). Thus, given applicants prior demonstration of structural similarity among homologous delta prime subunits of other *Bacillus species*, applicants respectfully submit that the genus of isolated DNA being claimed is adequately represented by the species of SEQ ID NO: 179 (encoding the delta prime subunit of SEQ ID NO:180).

Applicant's amendment and complete argument are acknowledged and have been carefully considered, however have been found to be non-persuasive in overcoming the instant rejection for the reasons previously made of record and repeated herein.

Applicant's amendment of Claim 1 to recite that "the encoded delta prime subunit can form a clamp loader complex" is helpful in further specifying the function of the encoded delta prime subunit, although not sufficient to overcome the rejection.

Notwithstanding the above functional aspect of the claimed delta prime subunits, it remains that the structural breadth of the claimed delta prime subunit encoding DNA is broader than applicants have adequately described. The basis of this is that while applicants have suggested that they have amended the claims such that the hybridization conditions, by which the claimed DNAs are limited, are more stringent, this remains unclear (See above rejection under 112 second paragraph). While certainly

applicant's amendment has resulted in a higher temperature, the still important constituents of "5X sodium citrate buffer" remain unclear.

Given the still loose association of the function and structure of the claimed genus, it remains that applicants have not adequately described the claimed genus of DNA molecules. Such is the case regardless of the relatedness of other delta prime subunits of other DNA polymerase III-type enzymes.

Thus it remains as to how the claimed function of the encoded delta prime subunits of a DNA polymerase type-III enzyme relate to the referred to structure.

Applicant is referred to the guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 2, 6-9 and 12-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 2, 6-9, 12-16 are further rejected under this statute because the newly added recitation of applicants hybridization conditions, of "comprising 5X sodium citrate buffer and at a temperature of 65°C, followed by washing in 5X sodium citrate buffer at 65°C" are not supported by applicants specification at the time of filing and thus considered new matter. It is noted that applicants did not point to support for this newly

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added recitation at the time of making the amendment and such support could not be located by the examiner. Thus this newly added recitation of these hybridization conditions is considered new matter.

Claims 1, 2, 6-9 and 12-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA molecule encoding a delta prime subunit of a DNA polymerase III-type enzyme, comprising the nucleotide sequence of SEQ ID NO: 179, does not reasonably provide enablement for any DNA molecule encoding any "delta prime subunit of a DNA polymerase III-type enzyme" from any *Bacillus* species, hybridizing to the complement of SEQ ID NO: 179 under conditions comprising 5X sodium citrate buffer and at a temperature of 65°C, followed by washing in 5X sodium citrate buffer at 65°C. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 1, 2 and 6-16. In response to this rejection, applicants have amended claims 1, canceled claims 10-11 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse the rejection on the basis that the present application provides the nucleotide sequence of *Bacillus stearothermophilus* *holB* (e.g., SEQ ID NO: 179) and describes how one of ordinary skill can isolate homologs of the disclosed sequence (see page 41, line 9 to page 42, line 29; Example 12), express the delta

prime subunit encoded by such homologous *holB* sequences (see Examples 12 and 22), and test the encoded delta prime subunit for activity (see Examples 26 and 30, using *Aquifex* delta prime subunit in assay). Thus, one of ordinary skill in the art would have been fully able to make and use DNA molecules and their encoded proteins within the scope of the presently claimed invention.

Applicants submit that for this reason, it should be apparent that the present application fully enables the production and use of other species of *Bacillus holB* homologs.

Applicants complete argument is acknowledged, however, is found non-persuasive for the reasons previously made of record and because applicants have not presented sufficient guidance with respect to the required function of the encoded proteins as well as the breadth of the structural limitations. Thus it remains that one of ordinary skill in the art would not be able to screen for such an activity, given the enormity of the claimed genus as defined structurally .

While it is recognized that one of skill could isolate naturally occurring homologs of the claimed DNAs, as applicants argue, it remains that applicants claims additionally encompass an even greater number of mutants and variants of the claimed DNA of SEQ ID NO: 179 and applicants specification combined with what is known in the art does not sufficiently enable the breadth of this genus. Thus, one of ordinary skill in the art would not have been fully able to make and use DNA molecules and their encoded proteins within the scope of the presently claimed invention.

Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the delta prime subunit activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those DNA molecules of the claimed genus encoding a protein having the desired activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any DNA molecule encoding a delta prime subunit of a DNA polymerase III-type enzyme from any *Bacillus* species, hybridizing to the complement of SEQ ID NO: 179 under conditions comprising 5X sodium citrate buffer and at a temperature of 65°C, followed by washing in 5X sodium citrate buffer at 65°C. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those DNA molecules having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rgH
3/15/2008

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652